REMARKS

I. Petition for Extension of Time

Applicants herewith petition the Commissioner for Patents to extend the time for response to the Office Action mailed 19 December 2007 for three (3) months from 19 March 2008 to 19 June 2008. Authorization is given to charge the extension of time fee of $1020.00 (37 C.F.R. §1.136 and §1.17) to Deposit Account No. 23-1703. Any deficiency or overpayment should be charged or credited to the above numbered deposit account.

II. Claim Amendments

Claim 1 has been canceled. The spelling of "gastroesophageal" has been corrected in amended claim 2. Claim 5 has been amended to recite that the salt of the esomeprazole compound of claim 2 is a sodium salt. The dependency of claims 3-8 has been amended in view of the cancellation of claim 1. Applicants submit that no new matter has been introduced by any of the claim amendments.

III. Claim Objections

The spelling of "gastroesophageal" has been corrected in amended claim 2 as suggested by the Examiner. Amended claims 4 and 5 are not duplicative as claim 4 is directed to the magnesium salt of the esomeprazole compound of claim 2 and claim 5 is directed to the sodium salt of that compound.

IV. Claim Rejections – 35 U.S.C. §112

The cancellation of claim 1 renders moot the rejection under 35 U.S.C. §112, first paragraph. Withdrawal thereof is requested.

V. Claim Rejections – 35 U.S.C. §103

Claims 2-9 are rejected under 35 U.S.C. §103(a) as being unpatentable over WO 98/54171 (hereinafter "Cotton") in view of the publication Murphy et al., "Sleep and the

Respiratory Complications of Gastroesophageal Reflux", Practical Gastroenterology, Vol. 17, 1993, pp. 16-29 (hereinafter "Murphy").

The claimed invention is directed to a method for improving sleep in a patient suffering from GERD by administering a therapeutically effective amount of esomeprazole to the patient in need thereof.

Cotton discloses that the magnesium salt of esomeprazole trihydrate may be used in the treatment of patients with symptomatic GERD. On page 7 of the Office Action, the Examiner acknowledges that Cotton does not disclose the use of the magnesium salt of esomeprazole trihydrate for improving sleep in a patient suffering from GERD. For that purpose, the Examiner relies on Murphy for the alleged disclosure that patients suffering from GERD also suffer from acid-induced arousal from sleep. The Examiner concludes that the combination of Cotton and Murphy serves as prior knowledge that the administration of esomeprazole in the treatment of GERD would have the effect of limiting intraesophageal acid, thereby reducing arousal from sleep.

The Examiner is correct that Cotton does not expressly disclose the administration of the magnesium salt of esomeprazole trihydrate for improving sleep in a patient suffering from GERD. And while Murphy may suggest that the administration of a proton pump inhibitor ("ppi"), e.g., omeprazole, may be an effective therapy in the treatment of GERD, Murphy fails to suggest which therapy would be the most effective therapy in the treatment of GERD and GERD-related sleep disturbances. In fact, Murphy lumps together so-called time-honored physical methods, medications and surgical procedures used to treat GERD (See page 20, second column, first full sentence; Table 3). As such, there is no suggestion that any one of the therapies listed in Table 3 would be more effective than the other in the treatment of GERD and GERD-related sleep disturbances.

Advantageously, the method of the claimed invention provides a therapy which is comparatively more effective in improving sleep in patients suffering GERD by the administration of esomeprazole. In support of the nonobviousness of the claimed invention, Applicants submit herewith three pages of a study published in 2003 comparing the efficacy of various ppis in the treatment of GERD. The titles of these publications are as follows:

1) Esomeprazole 40 mg Provides More Effective Intragastric Acid Suppression At Steady State Than Standard Doses Of Other Proton Pump Inhibitors;

2) Integrated Gastric Acidity to Evaluate Acid Suppression With Proton Pump Inhibitor Therapy: A Five-Way Crossover Comparison; and

3) Rationale For Changing Proton Pump Inhibitor Therapy: An Intraindividual Analysis of Gastric Acid Suppression Following Treatment With Different Proton Pump Inhibitors.

Although the publication date of the study is after the priority date of the subject application, the MPEP at §§716.01(d) and 2214.08 II(B) provides that ***the Examiner must consider all evidence*** traversing the rejection without any consideration of the actual date of the evidence:

MPEP §716.01(d) Weighing Objective Evidence [R-2]

IN MAKING A FINAL DETERMINATION OF PATENTABILITY, EVIDENCE SUPPORTING PATENTABILITY MUST BE WEIGHED AGAINST EVIDENCE SUPPORTING *PRIMA FACIE* CASE

When an applicant >timely< submits evidence traversing a rejection, the examiner must reconsider the patentability of the claimed invention. The ultimate determination of patentability must be based on consideration of the entire record, by a preponderance of evidence, with due consideration to the persuasiveness of any arguments and any secondary evidence *(cite)*. The submission of objective evidence of patentability does not mandate a conclusion of patentability in and of itself *(cite)*. Facts established by rebuttal evidence must be evaluated along with the facts on which the conclusion of a *prima facie* case was reached, not against the conclusion itself *(cite)*. In other words, each piece of rebuttal evidence should not be evaluated for its ability to knockdown the *prima facie* case. **All of the competent rebuttal evidence taken as a whole should be weighed against the evidence supporting the *prima facie* case** *(cite)*.

MPEP §2144.08 Obviousness of Species When Prior Art Teaches

II. B. Determining Whether Rebuttal Evidence Is Sufficient To Overcome the Prima Facie Case of Obviousness

Office personnel should consider all rebuttal arguments and evidence presented by applicants *(citations)*.

In accordance with the reported methodology of the study, the efficacy of esomeprazole in the inhibition of gastric acid secretion was compared with the following other ppis:

lansoprazole, omeprazole, pantoprazole and rabeprazole. The conclusion of the study is that esomeprazole provided the most effective intragastric acid suppression than the other ppis, including omeprazole. Therefore, the study substantiates that esomeprazole, when compared to other ppis, is the most effective ppi in limiting inraesophageal acid, and thereby comparatively more effective in reducing acid-induced arousal from sleep. This improvement is a surprising and unexpected advantage which the cited combination fails to suggest.

For all of the foregoing reasons, it is respectfully submitted that a *prima facie* case of obviousness has not been established. Withdrawal of the §103 rejection of claims 2- 9 is requested.

CONCLUSION

In view of the claim amendments and remarks herein, the application is in condition for allowance.

Authorization is hereby given to charge any fee due in connection with this communication to Deposit Account No. 23-1703.

Dated: 12 June 2008

Respectfully submitted,

/John M. Genova/
John M. Genova
Reg. No. 32,224

Customer No. 07470
Direct Line: (212) 819-8832

Enclosures:

1) Esomeprazole 40 mg Provides More Effective Intragastric Acid Suppression At Steady State Than Standard Doses Of Other Proton Pump Inhibitors;
2) Integrated Gastric Acidity to Evaluate Acid Suppression With Proton Pump Inhibitor Therapy: A Five-Way Crossover Comparison; and
3) Rationale For Changing Proton Pump Inhibitor Therapy: An Intraindividual Analysis of Gastric Acid Suppression Following Treatment With Different Proton Pump Inhibitors.